

AMENDMENTS TO THE CLAIMS

The text of all pending claims, (including withdrawn claims) is set forth below. Cancelled and not entered claims are indicated with claim number and status only. The claims as listed below show added text with underlining and deleted text with ~~strikethrough~~. The status of each claim is indicated with one of (original), (currently amended), (cancelled), (withdrawn), (new), (previously presented), or (not entered).

Please CANCEL claims 1-11, 16, 18, 20, 26 and 30 without prejudice or disclaimer.

Please AMEND claims 15, 24, 25, 28 and 31-34 in accordance with the following:

Claims 1-14 (Canceled).

15. (Currently amended) A method for ~~designing a system for~~ determining n target oligonucleotides, S_1, S_2, \dots, S_n , in for a plurality of sample samples, comprising:

(a) selecting or designing an ensemble of k probing units, P_1, P_2, \dots, P_k , each probing unit consisting of one or more probe oligonucleotide species having in combination one or more probing nucleotide sequences, wherein the one or more probing nucleotide sequences of at least one of the probing units can hybridize to target nucleotide sequences in at least two different target oligonucleotides;

(b) arranging the ensemble of said probing units, to be fixed on a solid substrate at a known coordinate on the substrate, in a manner allowing exposure to the sample under conditions permitting hybridization between corresponding target oligonucleotide and probe oligonucleotide sequences and allowing determination of an hybridization event and the extent of hybridization for each of the probe oligonucleotides;

(c) devising T being an $k \times n$ mathematical matrix consisting of components t_{ij} , in which matrix each t_{ij} denotes the affinity of hybridization of a target oligonucleotide S_i to probe oligonucleotides of probing unit P_j , under defined assay conditions, wherein said defined assay conditions are to be applied in the assay ~~(namely conditions to be eventually applied in the assay—type of medium, its content, temperature, etc.); and~~

(d) designating the T matrix as being associated with said ensemble to permit its use in determining expression of each of said target oligonucleotides;

(e) calculating a level of expression of each of the target oligonucleotides in an assayed sample can be calculated by applying the following vectorial equation (1):

$$c = Te$$

in which

c is a k-dimensional vector of values c_1, c_2, \dots, c_k , representing the level of hybridization of target oligonucleotides to each of probing units, P_1, P_2, \dots, P_k , respectively, and

e is an n-dimensional vector of values $(e_1, e_2, \dots, e_i, \dots, e_n)$, representing the level of expression of each of the target oligonucleotides S_1, S_2, \dots, S_n , respectively;

(f) calculating c for a first sample and for a second sample; and

(g) comparing c for said first sample and c for said second sample to determine a differential level of expression of said first and said second sample.

Claims 16-21 (Canceled).

22. (Previously Presented) A method according to claim 20 15, wherein the matrix T is a binary matrix.

23. (Previously Presented) A method according to claim 20 15, wherein the matrix T is a non-binary matrix.

24. (Currently Amended) A method according to claim 15, wherein said ensemble is an ensemble of k different probing units, for determining, by hybridization, n different target oligonucleotides in an assayed sample; each of said probing units ~~comprises~~ comprising one or more probe oligonucleotides with one or more probing nucleotide sequences and each of said

target oligonucleotides comprising one or more target nucleotide sequences, with the probing nucleotide sequences being capable of hybridizing to target nucleotide sequences, characterized in that the probing nucleotide sequences of at least one probing unit can hybridize to target nucleotide sequences in at least two different target oligonucleotides.

25. (Currently Amended) A method for determining relative abundances of n target oligonucleotides, S_1, S_2, \dots, S_n , ~~in an~~ for a plurality of sample assayed samples, comprising:

(a) providing an ensemble of k probing units, P_1, P_2, \dots, P_k , each probing unit consisting of one or more probe oligonucleotide species having in combination one or more probing nucleotide sequences, the probing units being selected such that at least one of the probing nucleotide sequences of at least one probing unit can hybridize to target nucleotide sequences in at least two different target oligonucleotides;

(b) exposing said ensemble to the assayed sample under hybridization-permissive conditions between corresponding target oligonucleotide and probe oligonucleotide sequences and measuring level of hybridization of target oligonucleotides from the assayed sample to each of the probing units;

(c) in the processor, devising a k -dimensional vector $c = (c_1, \dots, c_k)$, consisting of k coordinates c_j , with j being an integer from 1 to k , each of coordinates c_j being either (i) a representation of the level of hybridization of target oligonucleotides hybridized to probing unit P_j , or (ii) a representation of the difference between said level and a level measured in an identical ensemble exposed to a control sample in the same manner to that defined in step (b) ~~(in the latter case the vector c is in fact a product of subtraction of two vectors consisting each of results obtained from a different sample)~~;

(d) in the processor, calculating an n -dimensional vector e , consisting of n coordinates e_i , each of coordinates e_i being an indication of the level of target S_i in the sample, by solving the following vector equation (1):

$$c = T e$$

in which T is a $k \times n$ mathematical matrix consisting of components t_{ij} , in which matrix each t_{ij} denotes the affinity of hybridization of a target oligonucleotide S_i to probe oligonucleotides of probing unit P_j under the assay conditions;

(e) performing steps a-d for a plurality of samples; and

(f) determining a differential level of expression of said plurality of samples.

26-27. (Canceled).

28. (currently amended) A method according to claim 25, wherein the ensemble comprises also reference probing units and level of hybridization of target oligonucleotides to each probing unit[[s]] is compared to the level of hybridization of the target oligonucleotides to the reference probing units.

29. (Previously Presented) A method according to claim 25, wherein the probing units are immobilized on a substrate, each at a defined coordinate on the substrate.

30. (canceled)

31. (currently amended) A system for determining relative abundance of n target oligonucleotides, S_1, S_2, \dots, S_n , ~~in an~~ for a plurality of sample assayed samples, comprising:

(i) an ensemble of k probing units, P_1, P_2, \dots, P_k , each probing unit consisting of one or more probe oligonucleotide species having in combination one or more probing nucleotide sequences, the probing units being selected such that at least one of the probing nucleotide sequences of at least one probing unit can hybridize to target nucleotide sequences in at least two different target oligonucleotides;

(ii) detector for detecting a quantity indicating hybridization of a target oligonucleotide to a probing unit;

(iii) a processor coupled to said detector for constructing, based on the detected quantity, a k-dimensional vector $c = (c_1, \dots, c_k)$, consisting of k coordinates c_j , with j being an integer from 1 to k, each of coordinates c_j being either ~~([[[i]]])~~ a a representation of the level of target oligonucleotides hybridized to probing unit P_j , or ~~([[[i]]])~~ b a representation of the difference between said level and a level measured in an identical ensemble exposed to a control sample ~~in the same manner to that defined in step (b)~~; and for calculating an n-dimensional vector e, consisting of n coordinates e_i , each of coordinates e_i being an indication of the level of target S_i in the sample, by solving the following vector equation (1):

$$c = Te$$

in which T is a k x n mathematical matrix consisting of components t_{ij} , in which matrix each t_{ij} denotes the affinity of hybridization of a target oligonucleotide S_i to probe oligonucleotides of probing unit P_j under the assay conditions;

wherein the system is operative to calculate c for a plurality of samples for determining a differential level of expression of said plurality of samples.

32. (currently amended) A system according to claim 31, wherein in said ensemble at least one of the probe oligonucleotides has a probing sequence which is complementary to target sequences in at least two different target oligonucleotides.

33. (currently amended) A ~~combination~~ system for use in an assay for determining relative abundance of n target oligonucleotides, S_1, S_2, \dots, S_n , ~~in an~~ for a plurality of sample assayed samples, comprising:

(i) an ensemble of k probing units, P_1, P_2, \dots, P_k , each probing unit consisting of one or more probe oligonucleotide species having in combination one or more probing nucleotide

sequences, the probing units being selected such that at least one of the probing nucleotide sequences of at least one probing unit can hybridize to ~~[[a]]~~ target nucleotide sequences in at least two different target oligonucleotides;

(ii) a computer readable medium carrying data for inputting to a processor, which processor, based on ~~an inputted~~ input data constructs a vector $c = (c_1, \dots, c_k)$, consisting of k coordinates c_j , with j being an integer from 1 to k , each of coordinates c_j being either ~~([[i]])~~ a a representation of the level of target oligonucleotides hybridized to probing unit P_j , or ~~([[ii]])~~ b a value representing the difference between said level and a level measured in an identical ensemble exposed to a control sample ~~in the same manner to that defined in step (b)~~; calculates an n -dimensional vector e , consisting of n coordinates e_i , each of coordinates e_i being an indication of the level of target S_i in the sample, by solving the following vector equation (1):

$$c = Te$$

in which T is a $k \times n$ mathematical matrix consisting of components t_{ij} , in which matrix each t_{ij} denotes the affinity of hybridization of a target oligonucleotide S_i to probe oligonucleotides of probing unit P_j under the assay conditions;

wherein the system is operative to calculate c for a plurality of samples for determining a differential level of expression of said plurality of samples;

wherein said data on said data carrier comprises said matrix T which is associated for use with said ensemble.

34. (currently amended) A system ~~combination~~ according to claim 33, wherein in said ensemble at least one of the probe oligonucleotides has a probing sequence which is complementary to target sequences in at least two different target oligonucleotides.